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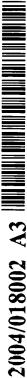
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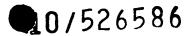
- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 17 June 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: USE OF GRANZYME B AS AN HSP70/HSP70 PEPTIDE DEPENDENT INDUCER OF APOPTOSIS IN TUMOR

(57) Abstract: The present invention relates to a method of inducing or enhancing the expression of granzyme B in natural killer (NK) cells. The present invention relates also to a use of said NK cells for the preparation of a pharmaceutical composition for the ireatment of tumors, viral or bacterial infections or inflammatory diseases. Further, the present invention relates to the use of granzyme B for the treatment of tumors, viral or bacterial infections or inflammatory diseases, wherein the tumor cells or the cells affected by said infection or inflammation express Hsp70 in their cell surface.





PATENT COOPERATION TREATY C'd PCT/PTO 23 FEB 2005

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER see Notification (Form PCT/ISA	of Transmittal of International Search Report /220) as well as, where applicable, item 5 below.
G1437 PCT International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/EP 03/09341	22/08/2003	23/08/2002
Applicant		
STEINECKE, peter		
This International Search Report has bee according to Article 18. A copy is being tr	n prepared by this international Searching At ansmitted to the International Bureau.	uthority and is transmitted to the applicant
This International Search Report consists It is also accompanied by	of a total of sheets. via copy of each prior art document cited in the	is report.
Basis of the report		
 With regard to the language, the language in which it was filed, un 	international search was carried out on the bless otherwise indicated under this item.	asis of the international application in the
the international search v Authority (Rule 23.1(b)).	vas carried out on the basis of a translation o	f the international application furnished to this
was carried out on the basis of th	e sequence listing:	international application, the international search
	onal application in written form.	
	ernational application in computer readable fo	om.
	this Authority in written form.	
	this Authority in computer readble form.	III. Tadas sataba
international application a	bsequently furnished written sequence listing as filed has been furnished.	
X the statement that the inf furnished	ormation recorded in computer readable form	is identical to the written sequence listing has been
2. X Certain claims were fou	ind unsearchable (See Box I).	
3. Unity of invention is lac	king (see Box II).	
4. With regard to the title,		•
X the text is approved as so	ubmitted by the applicant.	
the text has been establis	shed by this Authority to read as follows:	
5. With record to the chatrant		
5. With regard to the abstract,	ubmitted by the applicant.	
the text has been established	shed, according to Rule 38.2(b), by this Author e date of mailing of this international search r	ority as it appears in Box III. The applicant may, eport, submit comments to this Authority.
The figure of the drawings to be pub		
as suggested by the app		X None of the figures.
because the applicant fai		
because this figure bette	r characterizes the invention.	

Form PCT/ISA/210 (first sheet) (July 1998)



nal Application No PCT/EP 03/09341

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N5/08 A61K38/48 A61K35/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, MEDLINE, BIOSIS, CHEM ABS Data

	ENTS CONSIDERED TO BE RELEVANT		1
Category °	Citation of document, with Indication, where appropriate, of	the relevant passages	Relevant to claim No.
X	WO 99 49881 A (MULTHOFF GABRI 7 October 1999 (1999-10-07) cited in the application page 1, paragraph 1 page 3, paragraph 5 page 8, paragraph 2 -page 9, page 21 -page 26; examples 1-	paragraph 1	12,13, 16,22-24
X	US 6 261 839 B1 (MULTHOFF GAB 17 July 2001 (2001-07-17) column 1, line 65 -column 2, claims 1,19,20	•	12,13, 16,22-24
	ner documents are listed in the continuation of box C.	Patent family members are list	ed in annex.
A" docume conside earlier diling de which i citation O" docume other n P" docume later th	nt defining the general state of the art which is not ered to be of particular relevance ocument but published on or after the international ate nt which may throw doubts on priority claim(s) or scited to establish the publication date of another or other special reason (as specified) nt referring to an oral disclosure, use, exhibition or neans nt published prior to the international filing date but an the priority date claimed	 "T" later document published after the or priority date and not in conflict we cited to understand the principle or invention "X" document of particular relevance; the cannot be considered novel or can involve an inventive step when the "Y" document of particular relevance; the cannot be considered to involve an document is combined with one or ments, such combination being obtain the art. "&" document member of the same pate 	ith the application but theory underlying the e claimed invention not be considered to document is taken alone e claimed invention inventive step when the more other such docu- vious to a person skilled
Date of the a	ctual completion of the international search	Date of malling of the international s	search report
7	April 2004	23/04/2004	
ame and m	alling address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo ni, Fax: (+31–70) 340–3016	Authorized officer Sitch, W	



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Category °	citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; October 2001 (2001-10) MULTHOFF GABRIELE ET AL: "A 14-mer Hsp70 peptide stimulates natural killer (NK) cell activity" Database accession no. PREV200200042332 XP002276403 abstract & CELL STRESS AND CHAPERONES, vol. 6, no. 4, October 2001 (2001-10), pages 337-344, ISSN: 1355-8145			
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Internal Application No
PC17EP 03/09341

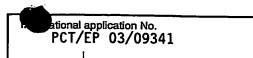
C.(Continue	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PC17EP 03/09341
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1997 HOMMEL-BERREY GRACE A ET AL: "Granzyme B independently of perforin mediates noncytolytic intracellular inactivation of vesicular stomatitis virus" Database accession no. PREV199799800859 XP002276404 abstract & CELLULAR IMMUNOLOGY, vol. 180, no. 1, 1997, pages 1-9, ISSN: 0008-8749	14,15, 17-24
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C (Continue	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/EP 0	3/09341
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T	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 17 October 2003 (2003-10-17) GROSS CATHARINA ET AL: "Cell surface-bound heat shock protein 70 (Hsp70) mediates perforin-independent apoptosis by specific binding and uptake of granzyme B." Database accession no. PREV200300583456 XP002276406 abstract		левчан ю саш по.
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PCT/ISAP10	. (Continuation of second sheet) (January 2004)		





Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1, 2, 9-11, 21-24 (all partially), and claims 3, 16-20 (all completely) are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

on patent family members

Internal Application No
PCITEP 03/09341

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